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09/485,421	10/05/2000	Sundarasamy Mahalingam	UPAP-0350	1903
34136	7590	04/06/2004	EXAMINER	
COZEN O'CONNOR, P.C. 1900 MARKET STREET PHILADELPHIA, PA 19103-3508			LI, QIAN JANICE	
			ART UNIT	PAPER NUMBER
			1632	

DATE MAILED: 04/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

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## Office Action Summary

### Application No.

09/485,421

### Applicant(s)

MAHALINGAM ET AL.

### Examiner

Q. Janice Li

### Art Unit

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2004.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-11 and 28-47 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 28-47 is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 20 February 2002 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All   b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                             | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____                                    |

### DETAILED ACTION

The amendment and response filed on 1/20/04 has been entered. Claims 1, 7, 28, 32, 37, 43 have been amended. Claims 1-11, and 28-47 are pending in the application and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims will not be reiterated. The arguments in 8/20/03 response would be addressed to the extent that they apply to current rejection.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

The prior rejection of claims 1, and 7-9 under 35 U.S.C. 102(e) as being anticipated by *Cohen et al* (USP 6,043,081) is withdrawn because applicant's argument is persuasive. *Cohen et al* teach a chimeric protein or a nucleic acid construct expressing the chimeric protein (e.g. fig. 13), but not a conjugated composition between

a fragment of a protein and a nucleic acid molecule.

Claims 1, 5-11 stand rejected under 35 U.S.C. 102(b) as being anticipated by WO9608970.

Applicants argue that the position of the Office is contrary to law and rules of the MPEP, and if one were to use the office's reasoning a species would never be patentable once a genus has been described citing *In re Baird* case law. Applicants go on to argue that one of skill in the art would not be able to instantly envisage fragment of Vpr that comprises residues 17-36 and/or 59-84.

The arguments have been fully considered but they are not persuasive for reasons of record and following.

The cited case law and the rules of MPEP acknowledge that a species claim does not itself render the species obvious over a genus. However, these rejected claims are not limited to a species (as are other allowed claims such as claims 28-47). The rejected claims are drawn to a genus encompassing any conjugate containing any Vpr fragment as long as it comprising residues 17-36 and/or 59-84. The claimed sequence of SEQ ID No: 1 comprises 96 amino acids, there are numerous fragments taught in the cited reference that would necessarily comprise the recited Vpr residues. This is because WO9608970 embraces any Vpr fragment that is more than five amino acids and has Vpr function, it does not place any limitation at the upper end for the length of the vpr fragment as long as it has the Vpr function, and has more than 5 amino acids. Clearly, numerous vpr fragments such as 2-95, 3-95, 4-95, ...16-95, and 1-94, 1-93, 1-

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92, 1-91, ...1-85 are encompassed by the teaching of *WO9608970*, these fragments ***always and necessarily*** comprise amino acid sequence 17-36 and/or 59-84. As long as one fragment comprises the recited fragments, the cited art anticipate the instant claims. The fact that there may be many other fragments that do not contain the recited residues does not obviate the anticipation.

Accordingly for reasons of record and set forth above, the rejection stands.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The prior rejection of claims 1-7, 10, and 11 under 35 U.S.C. 103(a) as being unpatentable over *Cohen et al* (US 6,043,081), in view of *Katz et al* (US 6,005,004) and *Zuckermann et al* (US 6,468,986) is withdrawn because *Cohen et al* teach a chimeric protein or a nucleic acid construct expressing the chimeric protein (e.g. fig. 13), but not a conjugated composition between a fragment of a protein and a nucleic acid molecule.

Claims 1-4 stand rejected under 35 U.S.C. 103(a) as being unpatentable over WO9608970, and further in view of *Katz et al* (US 6,005,004) and *Zuckermann et al* (US 6,468,986).

Applicants argue that there is no motivation to use the fragments of Vpr as recited, alone or in combination. Applicants also argue that finding the nuclear localization fragments within Vpr was unexpected and none of the references give direction as to the possible fragments of Vpr that would impel one of skill in the art to combine the reference. Applicants allege that the Office has selectively picked and chosen elements from all three references without using the references for what they fairly suggest.

The arguments have been fully considered but they are not persuasive for reasons of record and following.

It appears that Applicants are arguing that the cited references do not expressly suggest the claimed invention. However, it is well established in case law that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. In re Burkel, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered. The teaching of the cited references must be viewed in light of these factors.

With regard to the motivation, WO9608970 teaches that the *full length Vpr* or *functional fragments* thereof could be used for nucleus targeting of a therapeutic

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compound. This is a clear direction for using Vpr fragment. Accordingly, selecting a fragment that is a few amino acids shorter than the full length Vpr should generally be considered as a functional fragment of Vpr, many fragments generated this way would necessarily comprise residue 17-36 or 59-84. The fact that there may be many other fragments that do not contain these residues does not obviate the obviousness.

With regard to the picking and choosing, the title and focus of both *Katz et al* and *Zuckermann* are directed to compositions and methods for intracellular polynucleotide delivery, which is right on the subject matter of instant invention. Both *Katz et al* and *Zuckermann* clearly teach the means of chemical conjugation, such as covalent bounds, non-covalent bonds, and ionic bound for promoting nucleic acid cell entry. Thus, they not only fairly but also explicitly suggest the basis for combining the references, since the entry of cell nucleus first requires the entry of cells, any means that stabilizing the nucleic acid and promote cell entry would also facilitate the nucleus delivery. The instant situation is amenable to the type of analysis set forth in *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980) wherein the court held that it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose in order to produce a third composition that is to be used for the very same purpose since the idea of combining them flows logically from their having been individually taught in the prior art. Given the teaching of the prior art providing various means promoting nucleic acid stability and membrane permeability-all taught to be useful for delivering nucleic acid into cells, it would have been *prima facie* obvious to one of ordinary skill in the art to combine these compositions to generate a new composition

targeting a specific intracellular compartment for nucleic acid delivery with a reasonable expectation of success.

Accordingly, it is still deemed obvious to one of ordinary skill in the art at the time the invention was made to modify the methods of *WO9608970* by simply combining a polycationic amino acid in the composition of vpr conjugated nucleic acids, and using any known chemical bonding means as taught by *Katz et al* and *Zuckermann et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to do so because it was known that the addition of the polycationic molecule would enhance intracellular penetration of the therapeutic compound and reduce the degradation of nucleic acids during the delivery process. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

### ***Conclusion***

Claims 28-47 are allowable.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of



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the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Q. Janice Li** whose telephone number is 571-272-0730. The examiner can normally be reached on 9:30 am - 7 p.m., Monday through Friday, except every other Wednesday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Amy Nelson** can be reached on 571-272-0804. The fax numbers for the organization where this application or proceeding is assigned are **703-872-9306**.

Any inquiry of formal matters can be directed to the patent analyst, **Daniece Jacobs**, whose telephone number is (571) 272-0532.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist **Rena Jones** whose telephone number is **571-272-0571**.

**JANICE LI**  
**PATENT EXAMINER**



Q. Janice Li  
Patent Examiner  
Art Unit 1632



March 29, 2004